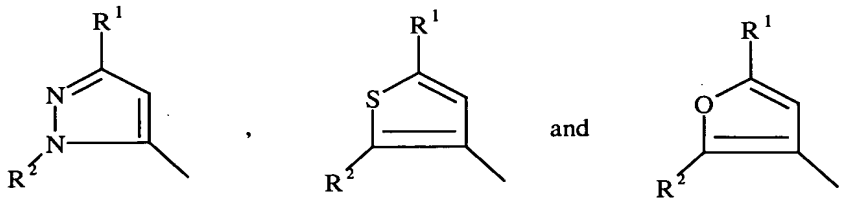


wherein R^1 is selected from the group consisting of C_3-C_{10} alkyl, C_3-C_{10} cycloalkyl, up to per-halosubstituted C_1-C_{10} alkyl and up to per-halosubstituted C_3-C_{10} cycloalkyl;

B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X_n,

wherein n is 0-3 and each X is independently selected from the group consisting of –CN, CO_2R^5, $-C(O)NR^5R^{5'}$, $-C(O)R^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, $C_{2\text{-}10}$-alkenyl, $C_{1\text{-}10}$-alkoxy, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_3-C_{13} heteroaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted $C_{2\text{-}10}$-alkenyl, substituted $C_{1\text{-}10}$-alkoxy, substituted C_3-C_{10} cycloalkyl, substituted C_4-C_{23} alkheteroaryl and -Y-Ar;

where X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NO_2$, $-NR^5C(O)R^{5'}$, $-NR^5C(O)OR^{5'}$ and halogen up to per-halosubstitution;

wherein R^5 and $R^{5'}$ are independently selected from H, C_1-C_{10} alkyl, $C_{2\text{-}10}$-alkenyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, up to per-halosubstituted C_1-C_{10} alkyl, up to per-halosubstituted $C_{2\text{-}10}$-alkenyl, up to per-halosubstituted C_3-C_{10} cycloalkyl, up to per-halosubstituted C_6-C_{14} aryl and up to per-halosubstituted C_3-C_{13} heteroaryl,

wherein Y is - O-, -S-, $-N(R^5)$-, $-(CH_2)_m$-, -C(O)-, -CH(OH)-, $-(CH_2)_mO$-, $-NR^5C(O)NR^5R^{5'}$-, $-NR^5C(O)$-, $-C(O)NR^5$-, $-(CH_2)_mS$-, $-(CH_2)_mN(R^5)$-, $-O(CH_2)_m$-, $-CHX^a$-, $-CX^a{}_2$-, $-S-(CH_2)_m$- and $-N(R^5)(CH_2)_m$-,

m = 1-3, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-C(O)NR^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-OC(O)R^5$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NO_2$, $-NR^5R^{5'}$, $-NR^5C(O)R^{5'}$ and $-NR^5C(O)OR^{5'}$, and

a1

wherein R^2 is C_6-C_{14} aryl, C_3-C_{14} heteroaryl, substituted C_6-C_{14} aryl or substituted C_3-C_{14} heteroaryl,

wherein if R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and V_n,

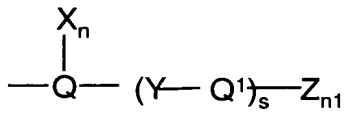
wherein n = 0-3 and each V is independently selected from the group consisting of -CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-C(O)R^5$, $-OC(O)NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-SO_2R^5$, $-SOR^5$, $-NR^5C(O)R^{5'}$, $-NO_2$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{24} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_6-C_{14} aryl, substituted C_3-C_{13} heteroaryl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{24} alkheteroaryl,

where V is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, -CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^5$, $-NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5C(O)R^{5'}$, $-NR^5C(O)OR^{5'}$ and $-NO_2$,

wherein R^5 and $R^{5'}$ are each independently as defined above.

4. A method of claim 1, wherein B is

a2



wherein

Y is selected from the group consisting of –O-, -S-, -CH_2-, -SCH_2-, -CH_2S-, -CH(OH)-, -C(O)-, -CX^a_2, -CX^aH-, -CH_2O- and -OCH_2-,

X^a is halogen,

Q is a six member aromatic structure containing 0–2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

a2

Q^1 is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members of the group consisting of N, O and S, substituted or unsubstituted by halogen up to per-halosubstitution,

s = 0 or 1, and

X, Z, n and n1 are as defined in claim 1.

12. A method according to claim 1, wherein R^1 is t-butyl.

a3

13. A method according to claim 12, comprising administering an amount of a compound of formula I effective to inhibit p38.

Please consider new claims 17-30.

--17. A method for the treatment of a disease other than cancer mediated by p38 which comprises administering a compound of formula I or a pharmaceutically acceptable salt thereof

I

a4

wherein B is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl substituted by -Y-Ar; and is optionally substituted by one or more substitutents independently selected from the group consisting of halogen, up to per-halosubstitution, and X_n,

wherein n is 0-3 and each X is independently selected from the group consisting of –CN, -CO_2R^5, -C(O)$NR^5R^{5'}$, -C(O)R^5, -NO_2, -OR^5, - SR^5, -$NR^5R^{5'}$, -$NR^5C(O)OR^{5'}$, -

$NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_1-C_{10} alkoxy, C_3-C_{10} cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl up to per halo-substituted C_1-C_{10} alkyl, up to per halo-substituted C_2-C_{10} alkenyl, up to per halo-substituted C_1-C_{10} alkoxy, up to per halo-substituted C_3-C_{10} cycloalkyl, and

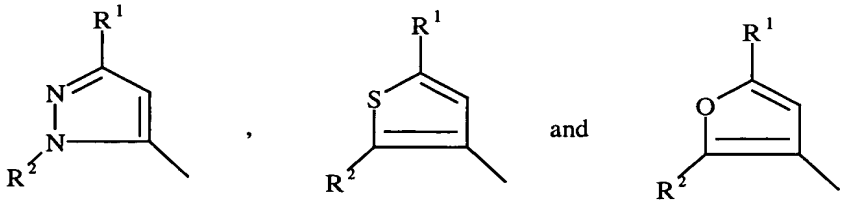
wherein R^5 and $R^{5'}$ are independently selected from H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_{10} cycloalkyl, up to per-halosubstituted C_1-C_{10} alkyl, up to per-halosubstituted C_2-C_{10} alkenyl and up to per-halosubstituted C_3-C_{10} cycloalkyl,

wherein Y is - O-, -S-, $-N(R^5)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-NR^5C(O)NR^5$ $NR^{5'}-$, $-NR^5C(O)-$, $-C(O)NR^5-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^5)-$, $-O(CH_2)_m-$, $-CHX^a$, $-CX^a{}_2-$, $-S-(CH_2)_m-$ and $-N(R^5)(CH_2)_m-$,

m = 1-3, and X^a is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of –CN, =O, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-C(O)-NR^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-C(O)R^5$, $-NR^5C(O)R^{5'}$, $-SO_2R^5$, $SO_2NR^5R^{5'}$, C_1-C_{10} alkyl, C_1-C_{10} alkoxyl, C_3-C_{10} cycloalkyl, up to per halo-substituted C_1-C_{10} alkyl, and up to per halo-substituted C_3-C_{10} cycloalkyl, and

wherein A is a heteroaryl selected from the group consisting of



wherein R^1 is selected from the group consisting of C_3-C_{10} alkyl, C_3-C_{10} cycloalkyl, up to per-halosubstituted C_1-C_{10} alkyl and up to per-halosubstituted C_3-C_{10} cycloalkyl,

wherein R^2 is C_6-C_{14} aryl, C_3-C_{14} heteroaryl, substituted C_6-C_{14} aryl or substituted C_3-C_{14} heteroaryl ,

wherein if R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and V_n,

wherein n = 0-3 and each V is independently selected from the group consisting of -CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-C(O)R^5$, $-OC(O)NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-SO_2R^5$, $-SOR^5$, $-NR^5C(O)R^{5'}$, $-NO_2$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{24} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_6-C_{14} aryl, substituted C_3-C_{13} heteroaryl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{24} alkheteroaryl,

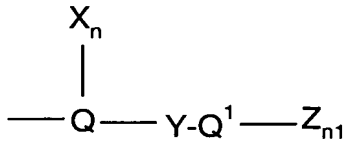
where V is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, -CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^5$, $-NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5C(O)R^{5'}$, $-NR^5C(O)OR^{5'}$ and $-NO_2$,

wherein R^5 and R^6 are each independently as defined above.

a4

18. A method as in claim 17 wherein R^2 is phenyl, substituted phenyl, pyridinyl or substituted pyridinyl.

19. A method of claim 17, wherein B is



wherein

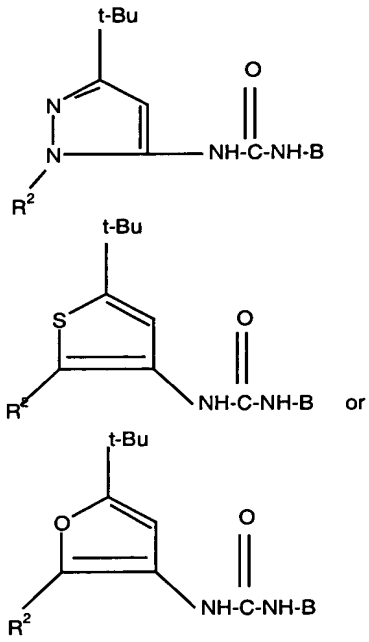
Y is as defined in claim 17,

Q and Q^1 are independently selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, optionally substituted by halogen, up to per-halo substitution, and

Z and X are independently selected from the group consisting of $-R^6$, $-OR^6$ and $-NHR^7$, wherein R^6 is hydrogen, C_1-C_{10}-alkyl or C_3-C_{10}-cycloalkyl and R^7 is selected from the group consisting of hydrogen, C_3-C_{10}-alkyl, and C_3-C_6-cycloalkyl wherein R^6 and R^7 can be substituted by halogen or up to per-halosubstitution.

20. A method as in claim 19, wherein Q is phenyl, Q^1 is phenyl or pyridinyl, Y is -O-, -S- or -CH_2, and X and Z are independently Cl, F, CF_3, NO_2 or CN.

21. A method as in claim 17, which comprises administering a compound of one of the formulae or a pharmaceuctically acceptable salt thereof:



a4

wherein B and R^2 are as defined in claim 17.

22. A method as in claim 21, wherein R^2 is phenyl, pyridinyl, substituted phenyl or substituted pyridinyl.

23. A method as in claim 17, comprising administering an amount of compound of formula I effective to inhibit p38.

24. A method as in claim 17, wherein the compound of formula I displays p38 activity (IC_{50}) better than 10μM as determined by an in-vitro kinase assay.

25. A method according to claim 17, wherein the disease is mediated by a cytokine or protease regulated by p38.

26. A method according to claim 17, wherein R^1 is t-butyl.

27. A method according to claim 26, comprising administering an amount of a compound of formula I effective to inhibit p38.

28. A method according to claim 17, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

29. A method according to claim 17, wherein the disease is an inflammatory or immunomodulatory disease.

30. A method according to claim 17, wherein the disease is rheumatoid arthritis, osteoarthritis, osteroporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions.--